

THE CLAIMS

What is claimed is:

- 5 1. A pharmaceutical composition which comprises venlafaxine derivative, or a pharmaceutically acceptable salt, solvate, or clathrate thereof, and a pharmaceutically acceptable carrier or excipient.
- 10 2. The pharmaceutical composition of claim 1 wherein the venlafaxine derivative is selected from the group consisting of (±)-O-desmethylvenlafaxine, (±)-N-desmethylvenlafaxine, (±)-N,O-didesmethylvenlafaxine, and (±)-N,N-didesmethylvenlafaxine.
- 15 3. The pharmaceutical composition of claim 2 wherein the venlafaxine derivative is (±)-O-desmethylvenlafaxine or (±)-N,O-didesmethylvenlafaxine.
4. The pharmaceutical composition of claim 1 adapted for intravenous infusion, transdermal delivery, or oral delivery.
- 20 5. The pharmaceutical composition of claim 1 wherein the venlafaxine derivative comprises a hydrochloride salt thereof.
6. The pharmaceutical composition of claim 1 wherein said pharmaceutically acceptable excipient comprises lactose, croscarmellose sodium, 25 microcrystalline cellulose, pre-gelatinized starch, and magnesium stearate.
7. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition is substantially free of all mono- or di-saccharides.
- 30 8. The pharmaceutical composition of claim 7 wherein said pharmaceutical composition is lactose-free.
9. The pharmaceutical composition of claim 1 wherein the venlafaxine derivative is (±)-O-desmethylvenlafaxine and the excipient comprises lactose.
- 35 10. The pharmaceutical composition of claim 9 wherein the excipient further comprises microcrystalline cellulose, pre-gelatinized starch, magnesium stearate, and croscarmellose sodium.

11. A pharmaceutical dosage form which comprises a therapeutically effective amount of venlafaxine derivative or a pharmaceutically acceptable salt, solvate, or clathrate thereof and a pharmaceutically acceptable carrier or excipient.

12. The dosage form of claim 11 wherein said dosage form is a tablet or a capsule.

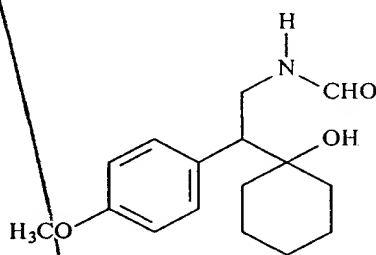
13. The dosage form of claim 11 adapted for intravenous infusion, transdermal delivery, or oral delivery.

14. The dosage form of claim 13 wherein the therapeutically effective amount is from about 10 mg to about 1000 mg.

15. The dosage form of claim 14 wherein the therapeutically effective amount is from about 50 mg to about 500 mg.

16. The dosage form of claim 15 wherein the therapeutically effective amount is from about 75 mg to about 350 mg.

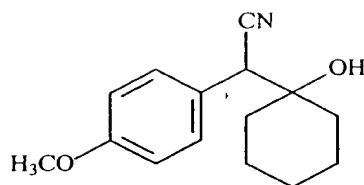
17. A method of preparing (\pm)-N-desmethylvenlafaxine which comprises contacting a compound of Formula 5:



with a reductant for a time and at a temperature sufficient to form (\pm)-N-desmethylvenlafaxine.

18. The method of claim 17 wherein the reductant is $\text{BH}_3 \cdot \text{Me}_2\text{S}$.

19. A method of preparing (\pm)-N,N-didesmethylvenlafaxine which comprises contacting a compound of Formula 2:



2

with a reductant for a time and at a temperature sufficient to form (±)-N,N-didesmethylvenlafaxine.

10

20. The method of claim 19 wherein the reductant is $\text{CoCl}_2/\text{NaBH}_4$.

15

21. A method of preparing (±)-O-desmethylvenlafaxine which comprises contacting (±)-venlafaxine with lithium diphenylphosphide for a time and at a temperature sufficient to form (±)-O-desmethylvenlafaxine.

20

22. Substantially pure (±)-O-desmethylvenlafaxine and pharmaceutically acceptable salts, solvates, and clathrates thereof.

23. Substantially pure (±)-N,O-didesmethylvenlafaxine and pharmaceutically acceptable salts, solvates, and clathrates thereof.

25

24. Substantially pure (±)-O-desmethyl-N,N-didesmethylvenlafaxine and pharmaceutically acceptable salts, solvates, and clathrates thereof.

25. (±)-N-desmethylvenlafaxine and pharmaceutically acceptable salts, solvates, and clathrates thereof.

30

26. (±)-N,N-didesmethylvenlafaxine and pharmaceutically acceptable salts, solvates, and clathrates thereof.

35

27. A method of treating an affective disorder in a human which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate, or clathrate thereof.

28. The method of treating an affective disorder in a human according to claim 27 in which said amount of venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof, is sufficient to alleviate the affective disorder but

insufficient to cause adverse effects associated with the administration of racemic venlafaxine.

5 29. The method of claim 27 wherein the affective disorder is selected from the group consisting of depression, attention deficit disorder, and attention deficit disorder with hyperactivity.

10 30. A method for treating obesity or weight gain in a human which comprises administering to a human in need of a reduction or maintenance in weight, a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

15 31. The method for treating obesity or weight gain in a human according to claim 30 wherein said amount is sufficient to alleviate obesity or weight gain but insufficient to cause the adverse effects associated with administration of racemic venlafaxine.

20 32. A method of treating disorders ameliorated by inhibition of neuronal monoamine reuptake in a human which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

25 33. The method of treating disorders ameliorated by inhibition of neuronal monoamine reuptake in a human according to claim 31 in which said amount is sufficient to alleviate said disorders but insufficient to cause adverse effects associated with administration of racemic venlafaxine.

30 34. The method of treating disorders ameliorated by inhibition of neuronal monoamine reuptake in a human according to claim 32 wherein said monoamine is dopamine.

35 35. The method of treating disorders ameliorated by inhibition of neuronal monoamine reuptake in a human according to claim 32 wherein said disorder is Parkinson's disease or epilepsy.

36. A method for treating cerebral function disorders in humans which comprises administering to a human in need of such treatment a therapeutically effective

amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

37. The method for treating cerebral function disorders in a human according to claim 35 wherein said amount is sufficient to alleviate cerebral function disorders but insufficient to cause adverse effects associated with administration of racemic venlafaxine.

38. The method for treating cerebral function disorders in a human according to claim 35 wherein said disorder is caused by a cerebrovascular disease.

39. The method for treating cerebral function disorders in a human according to claim 38 wherein said cerebrovascular disease is selected from the group consisting of cerebral infarction, cerebral bleeding, cerebral arteriosclerosis, cerebral venous thrombosis and head injuries.

40. The method for treating cerebral function disorders in a human according to claim 35 wherein said cerebral function disorder is selected from the group consisting of senile dementia, Alzheimer's type dementia, memory loss and amnesia/amnestic syndrome.

41. A method for treating pain in humans which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt thereof, solvate or clathrate thereof.

42. The method for treating pain in a human according to claim 41 wherein said amount is sufficient to alleviate pain but insufficient to cause adverse effects associated with administration of racemic venlafaxine.

43. The method for treating pain in a human according to claim 41 wherein the pain is chronic pain.

44. A method of treating an obsessive-compulsive disorder in a human, which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

45. A method of treating substance abuse in a human, which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

5 46. A method of treating or preventing pre-menstrual syndrome in a human, which comprises administering to a human in need of such treatment or prevention a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

10 47. A method of treating anxiety in a human which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

15 48. A method of treating an eating disorder in a human which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

20 49. A method of treating or preventing migraine, or migraine headaches, in a human which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

25 50. A method for treating or preventing incontinence in a human which comprises administering to a human in need of such treatment a therapeutically effective amount of a venlafaxine derivative, or a pharmaceutically acceptable salt, solvate or clathrate thereof.

30 51. The method of claim 50 wherein said incontinence is selected from the group consisting fecal incontinence, overflow incontinence, passive incontinence, reflex incontinence, stress urinary incontinence, urge incontinence, urinary exertional incontinence, and incontinence of urine.

35 52. The method of claim 27 wherein the venlafaxine derivative is selected from the group consisting of (±)-O-desmethylvenlafaxine, (±)-N-desmethylvenlafaxine, (±)-N,O-didesmethylvenlafaxine, and (±)-N,N-didesmethylvenlafaxine.

53. The method of claim 52 wherein the venlafaxine derivative is (±)-O-desmethylenlafaxine or (±)-N,O-didesmethylenlafaxine.

54. The method of claim 27 wherein venlafaxine derivative is administered by intravenous infusion, transdermal delivery, or orally as a tablet or a capsule.

55. The method of claim 27 wherein the amount administered is from about 10 mg to about 1000 mg per day.

56. The method of claim 55 wherein the amount administered is from about 50 mg to about 500 mg per day.

57. The method of claim 56 wherein the amount administered is from about 75 mg to about 350 mg per day.

58. The method of claim 27 wherein the venlafaxine derivative, or a pharmaceutically acceptable salt thereof, is administered together with a pharmaceutically acceptable carrier.

59. The method of claim 27 wherein the venlafaxine derivative is administered as a hydrochloride salt.